General

Guideline Title

VA/DoD clinical practice guideline for the management of concussion-mild traumatic brain injury.

Bibliographic Source(s)

Management of Concussion-mild Traumatic Brain Injury Working Group. VA/DoD clinical practice guideline for the management of concussion-mild traumatic brain injury. Version 2.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2016 Feb. 133 p. [130 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Department of Veterans Affairs, Department of Defense. VA/DoD clinical practice guideline for management of concussion/mild traumatic brain injury (mTBI). Washington (DC): Department of Veteran Affairs, Department of Defense; 2009 Apr. 112 p.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.

Recommendations

Major Recommendations

Note from the Department of Veterans Affairs and the Department of Defense (VA/DoD) and the National Guideline Clearinghouse (NGC): The

recommendations for the management of concussion-mild traumatic brain injury are organized into 2 modules with 2 algorithms (Module A: Initial Presentation [>7 Days Post-injury] and Module B: Management of Symptoms Persisting >7 days). The accompanying recommendations are presented below. See the original guideline document for the algorithms and evidence tables associated with selected recommendations, including level and quality of evidence, strength of recommendation, and supporting evidence citations.

The strength of recommendation grading (Strong For, Weak For, Strong Against, Weak Against) and recommendation categories (Reviewed, Not reviewed, New-added, New-replaced, Not changed, Amended, Deleted) are defined at the end of the "Major Recommendations" field.

Diagnosis and Assessment

1. The Work Group suggests using the terms "history of mild traumatic brain injury (mTBI)" or "concussion" and to refrain from using the terms "brain damage" or "patients with mTBI" in communication with patients and the public. (Weak For; Not reviewed, Amended)
2. The Work Group recommends evaluating individuals who present with symptoms or complaints potentially related to brain injury at initial presentation. (Strong For; Not reviewed, Amended)
3. Excluding patients with indicators for immediate referral, for patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, the Work Group suggests *against* using the following tests to establish the diagnosis of mTBI or direct the care of patients with a history of mTBI:
    a. Neuroimaging
    b. Serum biomarkers, including S100 calcium-binding protein B (S100-B), glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal esterase L1 (UCH-L1), neuron specific enolase (NSE), and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) peptide
    c. Electroencephalogram (EEG)

    (Weak Against; Reviewed, New-replaced)

4. The Work Group recommends *against* performing comprehensive neuropsychological/cognitive testing during the first 30 days following mTBI. For patients with symptoms persisting after 30 days, see Recommendation 17 below. (Strong Against; Not reviewed, Amended)
5. For patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, the Work Group recommends *against* using the following tests in *routine* diagnosis and care of patients with symptoms attributed to mTBI:
    a. Comprehensive and focused neuropsychological testing, including Automated Neuropsychological Assessment Metrics (ANAM), Neuro-Cognitive Assessment Tool (NCAT), or Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)

    (Strong Against; Reviewed, New-replaced)

6. For patients with new symptoms that develop more than 30 days after mTBI, the Work Group suggests a focused diagnostic work-up specific to those symptoms only. (Weak For; Not reviewed, Amended)

Co-occurring Conditions

7. The Work Group recommends assessing patients with symptoms attributed to mTBI for psychiatric symptoms and comorbid psychiatric disorders including major depressive disorder (MDD), posttraumatic stress disorder (PTSD), substance use disorders (SUD) and suicidality. Consult appropriate VA/DoD clinical practice guidelines. (Strong For; Not reviewed, Amended)

Treatment

8. The Work Group suggests considering, and offering as appropriate, a primary care, symptom-driven approach in the evaluation and management of patients with a history of mTBI and persistent symptoms. (Weak For; Not reviewed, Amended)

Effect of mTBI Etiology on Treatment Options and Outcomes

9. The Work Group recommends *not* adjusting treatment strategy based on mechanism of injury. (Strong Against; Reviewed, New-added)
10. The Work Group recommends *not* adjusting outcome prognosis based on mechanism of injury. (Strong Against; Reviewed, New-added)

Headache

11. The Work Group suggests that the treatment of headaches should be individualized and tailored to the clinical features and patient preferences. The treatment may include:
    a. Headache education including topics such as stimulus control, use of caffeine/tobacco/alcohol and other stimulants
    b. Non-pharmacologic interventions such as sleep hygiene education, dietary modification, physical therapy (PT), relaxation and modification of the environment (for specific components for each symptom, see Appendix B in the original guideline document)
    c. Pharmacologic interventions as appropriate both for acute pain and prevention of headache attacks

(Weak For; Reviewed, New-replaced)

Dizziness and Disequilibrium

12. In individuals with a history of mTBI who present with functional impairments due to dizziness, disequilibrium, and spatial disorientation symptoms, the Work Group suggests that clinicians offer a short-term trial of specific vestibular, visual, and proprioceptive therapeutic exercise to assess the individual's responsiveness to treatment. Refer to occupational therapy (OT), physical therapy (PT) or other vestibular trained care provider as appropriate. *A prolonged course of therapy in the absence of patient improvement is strongly discouraged.* (Weak For; Reviewed, Amended)

Tinnitus

13. There is no evidence to suggest for or against the use of any particular modality for the treatment of tinnitus after mTBI. (N/A; Reviewed, New-added)

Visual Symptoms

14. There is no evidence to suggest for or against the use of any particular modality for the treatment of visual symptoms such as diplopia, accommodation or convergence disorder, visual tracking deficits and/or photophobia after mTBI. (N/A; Reviewed, New-added)

Sleep Disturbance

15. The Work Group suggests that treatment of sleep disturbance be individualized and tailored to the clinical features and patient preferences, including the assessment of sleep patterns, sleep hygiene, diet, physical activities and sleep environment. The treatment may include, in order of preference:
    a. Sleep education including education about sleep hygiene, stimulus control, use of caffeine/tobacco/alcohol and other stimulants
    b. Non-pharmacologic interventions such as cognitive behavioral therapy specific for insomnia (CBTi), dietary modification, physical activity, relaxation and modification of the sleep environment (for specific components for each symptom see Appendix B in the original guideline document)
    c. Pharmacologic interventions as appropriate to aid in sleep initiation and sleep maintenance

    (Weak For; Reviewed, Amended)

Behavioral Symptoms

16. The Work Group recommends that the presence of psychological or behavioral symptoms following mTBI should be evaluated and managed according to existing evidence-based clinical practice guidelines, and based upon individual factors and the nature and severity of symptoms. (Strong For; Reviewed, Amended)

Cognitive Symptoms

17. The Work Group suggests that patients with a history of mTBI who report cognitive symptoms that do not resolve within 30 to 90 days and have been refractory to treatment for associated symptoms (e.g., sleep disturbance, headache) be referred as appropriate for a structured cognitive assessment or neuropsychological assessment to determine functional limitations and guide treatment. (Weak For; Not reviewed, Amended)
18. The Work Group suggests that individuals with a history of mTBI who present with symptoms related to memory, attention or executive function problems that do not resolve within 30 to 90 days and have been refractory to treatment for associated symptoms should be referred as appropriate to cognitive rehabilitation therapists with expertise in TBI rehabilitation. The Work Group suggests considering a short-term trial of cognitive rehabilitation treatment to assess the individual patient responsiveness to strategy training, including instruction and practice on use of memory aids, such as cognitive assistive technologies (AT). *A prolonged course of therapy in the absence of patient improvement is strongly discouraged.* (Weak For; Reviewed, New-replaced)
19. The Work Group suggests *against* offering medications, supplements, nutraceuticals or herbal medicines for ameliorating the neurocognitive effects attributed to mTBI. (Weak Against; Not reviewed, Amended)

<u>Setting of Care</u>

20. The Work Group suggests *against routine* referral to specialty care in the majority of patients with a history of mTBI. (Weak Against; Reviewed, Amended)
21. If the patient's symptoms do not resolve within 30 to 90 days and are refractory to initial treatment in primary care and significantly impact activities of daily living (ADLs), the Work Group suggests consultation and collaboration with a locally designated TBI or other applicable

specialist. (Weak For; Reviewed, Amended)

22. For patients with persistent symptoms that have been refractory to initial psychoeducation and treatment, the Work Group suggests referral to case managers within the primary care setting to provide additional psychoeducation, case coordination and support. (Weak For; Reviewed, Amended)
23. There is insufficient evidence to recommend for or against the use of interdisciplinary/multidisciplinary teams in the management of patients with chronic symptoms attributed to mTBI. (N/A; Reviewed, New-replaced)

Definitions

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

The grade of each recommendation is presented as part of a continuum:

- Strong For (or "The Work Group recommends offering this option …")
- Weak For (or "The Work Group suggests offering this option …")
- Weak Against (or "The Work Group suggests not offering this option …")
- Strong Against (or "The Work Group recommends against offering this option …")

Note that weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and clinician or they may be qualified with an explanation about the issues that would lead decisions to vary.

Recommendation Categories and Definitions

For use in the 2016 mTBI clinical practice guideline (CPG), a set of recommendation categories was adapted from those used by the United Kingdom National Institute for Health and Care Excellence (NICE). These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated.

Evidence Reviewed*	Recommendation Category*	Definition*
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012) and Garcia et al. (2014).

Abbreviation: CPG: clinical practice guideline

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Module A: Initial Presentation (>7 Days Post-injury)
- Module B: Management of Symptoms Persisting >7 days

Scope

Disease/Condition(s)

Concussion/mild traumatic brain injury (mTBI)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Rehabilitation

Treatment

Clinical Specialty

Family Practice

Neurological Surgery

Neurology

Physical Medicine and Rehabilitation

Psychiatry

Psychology

Sleep Medicine

Speech-Language Pathology

Intended Users

Advanced Practice Nurses

Nurses

Occupational Therapists

Physical Therapists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Social Workers

Speech-Language Pathologists

Guideline Objective(s)

- To assist providers in managing or co-managing patients with a history of mild traumatic brain injury (mTBI)
- To assist primary care providers in the management of all aspects of patient care, including, but not limited to, diagnosis, assessment, treatment and follow-up

Target Population

Adult patients aged 18 years or older with mild traumatic brain injury (mTBI) or a history of mTBI treated in any Department of Veterans Affairs (VA)/Department of Defense (DoD) clinical setting including Veterans as well as deployed and non-deployed active duty Service Members, and National Guard and Reserve components

Note: This Clinical Practice Guideline (CPG) does not address the following populations:

- Individuals in the immediate period (within seven days) following mTBI
- Individuals with moderate or severe TBI
- Children or adolescents

Interventions and Practices Considered

Diagnosis/Evaluation

1. Use of appropriate brain injury terminology when communicating with patients
2. Evaluation at initial presentation
3. Measurement of serum biomarkers, neuroimaging, and electroencephalography (not indicated routinely)
4. Comprehensive neuropsychological/cognitive testing for patients whose symptoms persist for more than 30 days
5. Focused diagnostic work-up specific to new symptoms
6. Assessment for co-morbid psychiatric disorders

Treatment/Management

1. Use of a primary care, symptom-driven management approach
2. Management of headache
    - Individualized, tailored treatment
    - Headache education
    - Non-pharmacologic interventions such as sleep hygiene education, dietary modification, physical therapy (PT), relaxation and modification of the environment
    - Pharmacologic interventions
3. Management of dizziness and disequilibrium
    - Vestibular, visual, and proprioceptive therapeutic exercise
    - Referral to occupational therapy (OT), PT or other vestibular trained care provider
4. Management of tinnitus
5. Management of visual symptoms
6. Management of sleep disturbance
    - Individualized, tailored treatment
    - Sleep education
    - Non-pharmacologic interventions such as cognitive behavioral therapy specific for insomnia (CBTi), dietary modification, physical activity, relaxation and modification of the sleep environment
    - Pharmacologic interventions

7. Management of behavioral symptoms according to established clinical practice guidelines
8. Management of cognitive symptoms
    - Referral for a structured cognitive assessment or neuropsychological assessment to determine functional limitations and guide treatment
    - Referral to cognitive rehabilitation therapists
9. Setting of care (primary care versus specialty care)

Note: The following were considered but not recommended: adjusting treatment approach and outcome prognosis based on mechanism of injury and medications, supplements, nutraceuticals or herbal medicines for management of cognitive symptoms.

Major Outcomes Considered

- Presence or intensity of symptoms attributed to mild traumatic brain injury (mTBI)
- Functional status
- Functional status predictive value for outcomes, or predictive value versus a gold standard
- Quality of life
- Severity of dizziness as measured by the Dizziness Handicap Inventory (DHI), Balance Error Scoring System (BESS) test, Berg Balance Scale (BBS), or other validated tests
- Severity of headache as measured by visual analog scales, the Oswestry Pain Scale, or other validated tools
- Safety/adverse events
- Functional attention, concentration, or memory, as measured by validated tools
- Severity of irritability, as reported by patient or family, using a validated tool
- Severity of insomnia, as measured by the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale, or other validated tools
- Severity of tinnitus, as measured by a standardized tinnitus questionnaire
- Symptoms of visual impairment, such as diplopia, visual tracking deficits, or photophobia

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Developing the Scope and Key Questions

The Clinical Practice Guideline (CPG) Champions, along with the Work Group, were tasked with identifying key evidence questions to guide the systematic review of the literature on mild traumatic brain injury (mTBI). These questions, which were developed in consultation with the Lewin team, addressed clinical topics of the highest priority for the Department of Veterans Affairs (VA) and Department of Defense (DoD) populations. The key questions (KQs) follow the population, intervention, comparison, outcome, timing and setting (PICOTS) framework for evidence questions, as established by the Agency for Healthcare Research and Quality (AHRQ). Table Aâ€1 in the original guideline provides a brief overview of the PICOTS typology.

The Champions and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the systematic evidence review. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. Table A-2 in the original guideline document contains the final set of KQs used to guide the systematic review for this CPG.

Conducting the Systematic Review

Extensive literature searches identified 3,259 citations potentially addressing the KQs of interest to this evidence review. Of those, 1,663 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date, not a full-length article). Overall, 1,596 abstracts were reviewed with 1,308 of those being excluded for the following reasons: not a systematic review or clinical study, did not address a KQ of interest to this review, did not enroll a population of interest, or

published prior to January 2008. A total of 288 full-length articles were reviewed. Of those, 193 were excluded at a first pass review for the following reasons: not addressing a KQ of interest, not enrolling the population of interest, not meeting inclusion criteria for clinical study or systematic review, not meeting inclusion criteria for any KQ, or being a duplicate. A total of 95 full-length articles were thought to address one or more KQs and were further reviewed. Of these, 51 were ultimately excluded for the reasons detailed in Figure A-1 in the original guideline document.

Overall, 42 studies (in 44 publications) addressed one or more of the KQs and were considered as evidence in the review. Table A-2 in the original guideline document indicates the number of studies that addressed each of the questions.

Criteria for Study Inclusion/Exclusion

General Criteria

- Clinical studies or systematic reviews published on or after January 1, 2008. If multiple systematic reviews addressed a KQ, the most recent and/or comprehensive review was selected. Clinical studies published subsequent to relevant systematic reviews were used to supplement the evidence base.
- Studies must have been published in English.
- Publication must be a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, and other publications that are not full-length, clinical studies were not accepted as evidence.
- Studies enrolled adults 18 years or older. In studies that mixed adults and children, at least 80% of the enrolled patients had to be 18 years or older.
- Studies must have enrolled ≥10 patients per treatment arm.
- Study must have reported on an outcome of interest.
- Study must have enrolled a patient population in which the most prevalent diagnosis is mTBI, with identifiable data for the population of interest (i.e., patients with a history of mTBI should be identifiable in the dataset). Studies that did not report separate data for mTBI were included only in the absence of other studies meeting this criterion, and only if the remaining patients in the study had moderate or severe TBI (not stroke). However, studies including at least 80% of patients with a history of mTBI were not required to report separate data for patients with a history of mTBI.

Key Question-Specific Criteria

- For KQ 1a, studies must have focused on use of specialized diagnostic approaches used at less than seven days following injury (acute period). For KQ 1b, studies must have focused on use of specialized diagnostic approaches at least seven days after the time of injury (post-acute period). Studies must have compared specialized diagnostic approaches to no test or usual care. For assessment of diagnostic accuracy, diagnostic cohort studies that compared a diagnostic test(s) to a reference standard within the same patient were acceptable.
- For KQ 2, non-randomized trials, cohort studies, case-controlled studies, and other observational studies were accepted as evidence in addition to randomized controlled trials (RCTs) and systematic reviews. Assessments must have been made at least seven days after the time of injury.
- For KQ 3, study must have been a systematic review of RCTs or an RCT. If insufficient evidence met this criterion, then controlled observational studies were considered as evidence for this question. Assessments must have been made at least seven days after the time of injury.
- For KQs 4–10, study must have been a systematic review of RCTs or an RCT. If insufficient evidence met this criterion, then controlled observational studies were considered as evidence for these questions. The minimum follow-up was three months.

Literature Search Strategy

ECRI Institute information specialists searched the following databases for relevant information. Search terms and strategies for the bibliographic databases appear below.

- Agency for Healthcare Research and Quality (AHRQ) 2008–March 2015 (U.S. Department of Health & Human Services)
- CINAHL 2008–March 2015 (EBSCO Host)
- Cochrane Library 2008–March 2015 (John Wiley & Sons, Ltd.)
- EMBASE (Excerpta Medica) 2008–March 2015 (Elsevier)
- Healthcare Standards (HCS) 2008–March 2015 (ECRI Institute)
- Medline 2008–March 2015 (OVID Technologies, Inc.)
- National Guideline Clearinghouse (NGC) 2008–March 2015 (Agency for Healthcare Research and Quality [AHRQ])
- National Institute for Health and Care Excellence (NICE) 2008–March 2015 (National Institute for Health and Care Excellence)

- PsycINFO 2008–March 2015 (OVID Technologies, Inc.)
- PubMed (In-process, Publisher, and PubMedNotMeSH records) 2008–March 2015 (National Library of Medicine [NLM])
- TRIP 2008–March 2015 (TRIP [Jon Brassey and Dr. Chris Price])

Key Question-Specific Search Strategies

Embase.com was used to search for unique EMBASE (EMTREE) records. OVID was used to simultaneously search Medline (MeSH) and PsycINFO. Similar strategies were used to search CINAHL and PubMed, as well as the ancillary databases listed above.

Specific search strings were used to capture studies based on the KQs identified by the mTBI Working Group. Unique strategies were structured for each question and pertain to diagnostic methods, mechanisms of injury, care settings, dizziness, headaches, impaired concentration and memory, behavioral problems, sleep disturbance, tinnitus, and vision impairment. These search results were further refined to capture specific study designs, publication types, date ranges, patient populations, English language studies, and to exclude out-of-scope citations.

See Tables A-4 through A-6 in the original guideline for topic-specific search terms and search strategies.

Number of Source Documents

Overall, 42 studies (in 44 publications) addressed one or more of the key questions and were considered as evidence in the review. See Figure A-1 in the original guideline document for a study flow diagram.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence and Definitions*

High quality — Further research is very unlikely to change confidence in the estimate of effect.
Moderate quality — Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low quality — Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low quality — Any estimate of effect is very uncertain.

*Guyatt, G. H., Oxman, A. D., Vist, G. E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., Schünemann, H. J. & the GRADE Working Group. (2008). GRADE; An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ, 336*, 924-926.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Abstracting and Managing Data

For each study included in the systematic review, the following study level details were abstracted: country, purpose, and quality rating. For previous systematic reviews, the review team reported the search strategy used, study selection criteria, and overall information about the evidence base, including number of included studies and overall patients enrolled. For all studies, the reviewers abstracted data about characteristics of the included patients and interventions being assessed.

Assessing Individual Studies' Methodological Quality (i.e., Internal Validity or Risk of Bias)

As per the Department of Veterans Affairs/Department of Defense (VA/DoD) *Guidelines for Guidelines* document (see the "Availability of Companion Documents" field), risk-of-bias (or study quality) of individual studies and previous systematic reviews was assessed using the U.S. Preventive Services Task Force (USPSTF) method. Each study was assigned a rating of Good, Fair, or Poor based on sets of criteria that vary depending on study design. Detailed lists of criteria and definitions of Good, Fair, or Poor ratings for different study designs appear in Appendix VII of the USPSTF procedure manual.

Data Synthesis

A narrative approach to synthesizing the evidence for all the Key Questions (KQs) was used. As indicated in the VA/DoD *Guidelines for Guidelines* document, the first line of evidence was previous systematic reviews. For questions in which a previous review was available, individual studies that met the systematic review's inclusion criteria were used to supplement or update the previous review. Reviewers considered whether subsequent evidence supports the conclusions reported in the previous review. For questions for which no previous review was available, the overall findings for the outcomes of interest of the studies that addressed a KQ were summarized.

Assessing the Overall Quality of the Body of Evidence for an Outcome

The overall quality of the body of evidence supporting the findings for the outcomes of interest in this report was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. The GRADE system primarily involves consideration of the following factors: overall study quality (or overall risk of bias or study limitations), consistency of evidence, directness of evidence, and precision of evidence. Given time and resources, other factors such as publication bias may also be considered. For more information on the GRADE system go to the GRADE working group Web site.

The GRADE system rates the overall quality of the evidence as High, Moderate, Low, and Very Low (see the "Rating Scheme for the Strength of the Evidence" field). The overall quality of a body of evidence is rated based on the factors described in Table 1 in the systematic review. For instance, a body of evidence that consists of randomized controlled trials (RCTs) automatically starts with a rating of high quality. This rating can be downgraded if some of the RCTs have serious flaws such as lack of blinding of outcome assessors, not reporting concealment of allocation, or high dropout rate. Similarly, the quality can be downgraded or further downgraded if inconsistencies of findings are present or if there is a lack of precision surrounding an outcome's effect size.

Assessing Applicability

When describing the evidence base addressing a KQ, the evidence review team discussed aspects of the included studies, such as characteristics of included patients and treatments being assessed that may make the overall findings of the studies more or less applicable to the population, treatments, or outcomes of interest to this review.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Methods

The current guideline is an update to the 2009 mild traumatic brain injury (mTBI) clinical practice guideline (CPG). The methodology used in developing the 2016 CPG follows the *Guideline for Guidelines*, an internal document of the Department of Veterans Affairs/Department of Defense (VA/DoD) Evidence-Based Practice Working Group (EBPWG) (see the "Availability of Companion Documents" field). This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts from within the VA and DoD, known as the Work Group, and ultimately, the development and publication of an updated mTBI CPG.

The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations, as well as writing and publishing a guideline document to be used by providers within the VA/DoD healthcare system. Specifically, the Champions and the Work Group members for this guideline were responsible for identifying the key questions (KQs) of the greatest clinical relevance, importance, and interest for the management of patients with a history of mTBI. The amount of new scientific evidence that had accumulated since the previous version of the CPG was also taken into consideration in the identification of the KQs. The Champions and the Work Group also provide direction

on inclusion and exclusion criteria for the evidence review and assessed the level of quality of the evidence. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

The VA Office of Quality, Safety and Value, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified three clinical leaders as Champions for the 2016 CPG.

The Lewin Team (Team), including The Lewin Group, Duty First Consulting, ECRI Institute, and Sigma Health Consulting, LLC, was contracted by the VA and DoD to support the development of this CPG and conduct the evidence review. The team held the first conference call in December 2014, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality, Safety and Value and the DoD Office of Evidence Based Practice, and the Champions. During this call, the project team discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review about the management of mTBI. The group also identified a list of clinical specialties and areas of expertise that are important and relevant to the management of mTBI, from which Work Group members were recruited. The specialties and clinical areas of interest included: blind rehabilitation, family medicine, occupational therapy (OT), language neurology, nursing, pharmacy, physical medicine and rehabilitation (PM&R), physical therapy (PT), polytrauma care, primary care, psychiatry, psychology, and speech-language pathology.

The guideline development process for the 2016 CPG update consisted of the following steps:

1. Formulating and prioritizing KQs for the systematic review
2. Conducting the systematic review
3. Convening a face-to-face meeting with the CPG Champions and Work Group members
4. Drafting and submitting a final CPG about the management of mTBI to the VA/DoD EBPWG

Appendix A in the original guideline document provides a detailed description of each of these tasks.

Convening the Face-to-face Meeting

In consultation with the COR, the Champions, and the Work Group, the Lewin Team convened a three and a half day face-to-face meeting of the CPG Champions and Work Group members on June 29–July 2, 2015. These experts were gathered to develop and draft the clinical recommendations for an update to the 2009 mTBI CPG. Lewin presented findings from the evidence review of KQs 1-10 in order to facilitate and inform the process.

Under the direction of the Champions, the Work Group members were charged with interpreting the results of the evidence review, and asked to review, assess, and categorize recommendations from the 2009 mTBI CPG. The members also developed new clinical practice recommendations not present in the 2009 mTBI CPG, based on the 2015 evidence review. The subject matter experts were divided into three smaller subgroups at this meeting.

As the Work Group members drafted clinical practice recommendations, they also assigned a grade for each recommendation based on a modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) and U. S. Preventive Services Task Force (USPSTF) methodology. Each recommendation was graded by assessing the quality of the overall evidence base, the associated benefits and harms, the variation in values and preferences, and other implications of the recommendation.

Grading Recommendations

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a grade for the strength of each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Values and preferences
- Other implications, as appropriate, include:
    - Resource Use
    - Equity
    - Acceptability
    - Feasibility

- Subgroup considerations

The framework presented in Table A-7 in the original guideline document was used by the Work Group to guide discussions on each domain.

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework in Table A-7, which combines the four domains. GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances where strong recommendations are warranted even when the quality of evidence is low. In these types of instances where the balance of desirable and undesirable outcomes and values and preferences played large roles in determining the strength of a recommendation, this is explained in the discussion section for the recommendation.

The GRADE of a recommendation (see the "Rating Scheme for the Strength of the Recommendations" is based on the following elements:

- Four decision domains used to determine the strength and direction
- Relative strength (Strong or Weak)
- Direction (For or Against)

Reconciling 2009 CPG Recommendations

Evidence-based CPGs should be current, which typically requires revisions based on new evidence or as scheduled subject to time-based expirations. For example, the USPSTF has a process for refining or otherwise updating its recommendations pertaining to preventive services. Further, the inclusion criteria for the National Guideline Clearinghouse (NGC) specify that a guideline must have been developed, reviewed, or revised within the past five years.

The mTBI Guideline Work Group focused largely on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Guideline Work Group considered the current applicability of other recommendations that were included in the previous 2009 mTBI CPG, subject to evolving practice in today's environment.

A set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE, UK). These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated. In brief, the categories took into account whether or not the evidence that related to a recommendation was systematically reviewed as part of the update, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current patient care environment and inside the scope of the CPG (see the "Rating Scheme for the Strength of the Recommendations" field). Additional information regarding these categories and their definitions can be found in Appendix A in the original guideline document. The categories for the recommendations included in the 2016 version of the guideline are noted in the "Major Recommendations" field.

Because the 2009 mTBI CPG was developed using an evidence-rating method (USPSTF method) differing from the methodology currently used (GRADE method), the CPG Work Group recognized the need to accommodate the transition in evidence rating systems from the 2009 mTBI CPG to the current CPG. In order to report the strength of all recommendations using a consistent format (i.e., the GRADE system) the CPG Work Group converted the USPSTF strengths of the recommendation accompanying the carryover recommendations from the 2009 guideline to the GRADE system. As such, the CPG Work Group considered the strength of the evidence cited for each recommendation in the 2009 mTBI CPG as well as harms and benefits, values and preferences, and other implications, where appropriate. The CPG Work Group referred to the available evidence as summarized in the body of the 2009 mTBI CPG and did not assess the evidence review systematically that was conducted for the 2009 mTBI CPG. In some instances, selected peer-reviewed literature published since the 2009 mTBI CPG was considered along with the evidence base used for that CPG. When newer literature was considered in converting the strength of the recommendation from the USPSTF to GRADE system, it is referenced in the discussion of the corresponding recommendation, as well as in Appendix D in the original guideline document.

The CPG Work Group recognizes that, while there are practical reasons for incorporating findings from a previous systematic review, previous recommendations, or recent peer-reviewed publications into an updated CPG, doing so does not involve an original, comprehensive systematic review and, therefore, may introduce bias. In contrast, the recommendations labeled as "Reviewed" were based on a new or an updated systematic review of the literature.

Drafting and Submitting the Final CPG

Following the face-to-face meeting, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2009 mTBI CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2009 mTBI CPG for inclusion in

the update. During this time, the Champions and Work Group also made additional revisions to the algorithms, as necessary.

Rating Scheme for the Strength of the Recommendations

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

The grade of each recommendation is presented as part of a continuum:

- Strong For (or "The Work Group recommends offering this option …")
- Weak For (or "The Work Group suggests offering this option …")
- Weak Against (or "The Work Group suggests not offering this option …")
- Strong Against (or "The Work Group recommends against offering this option …")

Note that weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and clinician or they may be qualified with an explanation about the issues that would lead decisions to vary.

Recommendation Categories and Definitions

For use in the 2016 mild traumatic brain injury clinical practice guideline, a set of recommendation categories was adapted from those used by the United Kingdom National Institute for Health and Care Excellence (NICE). These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated.

Evidence Reviewed*	Recommendation Category*	Definition*
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012) and Garcia et al. (2014).

Abbreviation: CPG: clinical practice guideline

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

After developing the initial draft of the updated clinical practice guideline (CPG), an iterative review process was used to solicit feedback on and make revisions to the CPG. Once they were developed, the first two drafts of the CPG were posted on a wiki Web site for a period of 14 to 20 business days for internal review and comment by the Work Group. All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG.

Draft 3 of the CPG was made available for peer review and comment. This process is described in the "Peer Review Process" section in the original guideline document. After revisions were made based on the feedback received during the peer review and comment period, the Champions presented the CPG to the Evidence-Based Practice Working Group (EBPWG) for their approval. Changes were made based on feedback from the EBPWG and the guideline was finalized.

The final 2016 mild traumatic brain injury (mTBI) CPG was submitted to the EBPWG in January 2016.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

Table A-2 in the original guideline documents indicates the number and type of studies that addressed each of the questions. The evidence base consists primarily of systematic reviews and randomized controlled trials.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Improved treatment and management of patients with a history of mild traumatic brain injury (mTBI) who present for care in the Department of Veterans Affairs (VA) and Department of Defense (DoD)

Refer to the "Discussion" sections following each recommendation in the original guideline document for information on the balance between benefits and harms for specific recommendations.

Potential Harms

- Patients with a history of traumatic brain injury (TBI) can be more sensitive to side effects of medications used in symptom management. Watch closely for toxicity and drug-drug interactions and assess regularly for side effects.
- Limit quantities of medications with high risk for suicide as the suicide rate is higher in the TBI population.
- Educate patients and family/care givers to avoid the use of alcohol with medications.
- Minimize caffeine and avoid herbal or diet supplements such as "energy" products as some contain agents that cross-react with the psychiatric medications and lead to a hypertensive crisis.
- Combination drugs used for treatment of posttraumatic headache should not be used more than two days a week due to side effect concerns and the potential for dependency. When using any medications, caution must be taken to avoid overuse and subsequent rebound headaches.
- Refer to Tables B-3 and B-4 in the original guideline document for adverse drug effects associated with abortive and prophylactic migraine medications.
- Refer to Table B-6 in the original guideline document for adverse drug effects associated with sleep agents.

- It is unknown if the benefits outweigh the harms or burden of involving TBI specialists in patient symptom management or interventions to improve performance of activities of daily living (ADLs). Increasing the number of specialists involved in care, even if optimally coordinated, increases the likelihood of differences in clinical opinions, conflicting patient education messages, or potential for risks such as medication interactions.

Refer to the "Discussion" sections following each recommendation in the original guideline document for additional information on the balance between benefits and harms for specific recommendations.

Contraindications

Contraindications

- Medications that lower the seizure threshold (e.g., bupropion, traditional antipsychotic medications) or those that can cause confusion (e.g., lithium, benzodiazepines, anticholinergic agents) should be avoided in the traumatic brain injury (TBI) population.
- The use of benzodiazepines should be avoided in patients with a history of mild TBI due to potential development of dependency and worsening of other persistent symptoms such as cognitive changes and decision making ability, as well as a high likelihood to worsen comorbid health conditions if present (particularly depression or posttraumatic stress disorder [PTSD]).

Qualifying Statements

Qualifying Statements

- The Department of Veterans Affairs (VA) and the Department of Defense (DoD) guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.
- Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.
- These guidelines are not intended to represent TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Implementation of the Guideline

Description of Implementation Strategy

This Clinical Practice Guideline (CPG) and associated algorithms were designed to be adapted by individual healthcare providers with consideration of local needs and resources. The algorithms serve as tools to prompt providers to consider key decision points in the course of an episode of care. Within the body of the CPG, the recommendations offer evidence-based guidance for the care of patients with a history of mild traumatic brain injury (mTBI). Appendix B in the original guideline also offers users of the CPG a symptom-based clinical guide to best practices that have been reviewed by the Work Group. It should be noted that this material is set apart from the body of the CPG because it is based on expert consensus and common clinical practice. In addition, a clinician summary, clinician pocket card, and patient guide were developed to accompany this CPG to facilitate use of the content (see the "Availability of Companion Documents" field).

Implementation Tools

Clinical Algorithm

Patient Resources

Pocket Guide/Reference Cards

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Management of Concussion-mild Traumatic Brain Injury Working Group. VA/DoD clinical practice guideline for the management of concussion-mild traumatic brain injury. Version 2.0. Washington (DC): Department of Veterans Affairs, Department of Defense; 2016 Feb. 133 p. [130 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb

Guideline Developer(s)

Department of Defense - Federal Government Agency [U.S.]

Department of Veterans Affairs - Federal Government Agency [U.S.]

Veterans Health Administration - Federal Government Agency [U.S.]

Source(s) of Funding

Guideline Committee

The Concussion/Mild Traumatic Brain Injury (mTBI) Guideline Working Group

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Financial Disclosures/Conflicts of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest in the past two years, including verbal affirmations of no conflict of interest at regular meetings. The project team was also subject to random Web-based surveillance (e.g., ProPublica). If there was a positive (yes) conflict of interest response (actual or potential), then action was taken by the co-chairs and evidence-based practice program office, based on the level and extent of involvement, to mitigate the conflict of interest. Actions ranged from restricting participation and/or voting on sections related to a conflict, to removal from the Work Group. Recusal was determined by the individual, co-chairs, and the Office of Evidence Based Practice.

Noted conflict of interest disclosures:

- COL Sidney Hinds II, MD, has previously served on the National Football League (NFL) Head Trauma Advisory Board; however, over 12 months has elapsed since this engagement.
- Scott McDonald, PhD, is involved in traumatic brain injury (TBI) research that is funded by the Department of Veterans Affairs (VA) and by General Dynamics.

The above disclosures were brought forward by the individuals and evaluated by VA/Department of Defense (DoD) leadership. Given the nature of the disclosures, the Work Group members were authorized to continue work on the clinical practice guideline (CPG) in an unrestricted capacity.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Department of Veterans Affairs, Department of Defense. VA/DoD clinical practice guideline for management of concussion/mild traumatic brain injury (mTBI). Washington (DC): Department of Veteran Affairs, Department of Defense; 2009

Apr. 112 p.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Department of Veterans Affairs (VA) Web site .

Availability of Companion Documents

The following are available:

- VA/DoD clinical practice guideline for the management of concussion-mild traumatic brain injury. Clinician summary. Washington (DC): Department of Veterans Affairs, Department of Defense; 2016 Feb. 53 p. [88 references]. Available from the Department of Veterans Affairs (VA) Web site .
- VA/DoD clinical practice guideline for the management of concussion-mild traumatic brain injury. Pocket card. Washington (DC): Department of Veterans Affairs, Department of Defense; 2016 Feb. 6 p. Available from the VA Web site .
- Guideline for guidelines. Washington (DC): Department of Veterans Affairs; 2013 Apr 10. Available from the VA Web site .
- Putting clinical practice guidelines to work in VHA. Washington (DC): Department of Veterans Affairs. 64 p. Available from the VA Web site .

In addition, information on clinical symptom management and mechanism of injury is available in appendices of the original guideline document .

Patient Resources

The following is available:

- VA/DoD clinical practice guideline for the management of concussion-mild traumatic brain injury. Patient summary. Washington (DC): Department of Veterans Affairs, Department of Defense; 2016 Feb. 3 p. [3 references]. Available from the Department of Veterans Affairs (VA) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This summary was completed by ECRI Institute on June 24, 2010. This summary was updated by ECRI Institute on July 22, 2016. The information was not verified by the guideline developer. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

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